

1

## REVERSIBLE HYDROGEL SYSTEMS AND METHODS THEREFOR

The present invention claims priority to U.S. Provisional Patent Application Ser. No. 60/425,764, filed Nov. 13, 2002.

### FIELD OF THE INVENTION

The present invention relates to reversible hydrogel systems. Particularly, the hydrogel of the present invention is made up of copolymers that can be a hydrogel when in an oxidized state and can be a solution when in a reduced state. A solution of the copolymer can be oxidized to form a hydrogel; and the hydrogel can be reduced to form a solution of the copolymer. The solution can be dehydrated to produce the dry copolymer for storage. Furthermore, the present invention also relates to methods of making and using the reversible hydrogel systems.

### BACKGROUND OF THE INVENTION

A cataract is a cloudy or opaque area in the normally transparent crystalline lens of the eye. As the opacity increases, it prevents light rays from passing through the lens and focusing on the retina, the light sensitive tissue lining the back of the eye. Early lens changes or opacities may not disturb vision, but as the lens continues to change, several specific symptoms may develop including blurred vision, sensitivity to light and glare, increased nearsightedness, and/or distorted images in either eye.

There are no medications, eye drops, exercises, or glasses that will cause cataracts to disappear once they have formed. When a person is unable to see well enough to perform normal everyday activities, surgery is required to remove the cataract and restore normal vision.

In modern cataract extraction surgery, the cataract is removed from the lens through an opening in the lens capsule. Using an operating microscope, a small incision is made into the eye, and subsequently, the lens capsule. Microsurgical instruments are used to first fragment and then suction the cloudy lens from the eye. The back membrane of the lens (called the posterior capsule) is left in place. The focusing power of the optical system is then restored, usually only for distant vision, by replacement with a permanent pre-fabricated clear plastic intraocular lens (IOL) implant which became popular in the early 1980s.

Prior to the development of IOLs, cataract patients were forced to wear thick "coke bottle" glasses or contact lenses after surgery. Unfortunately, vision is not very good with thick eyeglasses and thick contact lenses do not provide a much better option. The discovery of IOLs solved this problem.

Intraocular lenses can be divided into two main groups: non-foldable and foldable. The original intraocular lenses were made from a hard plastic (non-foldable) material and could therefore be introduced into the eye only with an incision as large as the diameter of the lens. In order to reduce the trauma to the eye in cataract surgery, it is desirable to keep the incision through which the surgical procedure is conducted as small as possible. Foldable lenses are made of acrylic or silicone and can be rolled up and placed inside a tiny tube. The tube is inserted through a very small incision, less than 2.5 mm in length. Once inside the eye, the IOL gently unfolds.

Before the cataract surgery is performed, the corneal curvature and the axial length of the eye of the patient is measured to determine the proper focal power for the IOL that will be inserted. Using sophisticated formulas to calculate the

2

corrective prescription power of the lens, the IOL not only replaces the need for thick glasses, but it can also correct the existing refractive error of the eye.

Although standard IOLs are available in a variety of focal lengths, those lengths are fixed for any given lens. Thus, unlike the natural lens of the eye, a standard IOL is unable to change focus. Therefore, the patient who must rely upon a standard IOL loses accommodative capability after surgery. IOLs are usually chosen that provide adequate distance vision. However, if distance vision is clear, then near vision may be blurred and the patient may require the use of reading glasses following cataract surgery.

Bifocal and multifocal IOLs have been developed to correct this problem. Although they are able to reduce or even eliminate the need for reading glasses, these IOLs produce a reduction in contrast sensitivity and the subjective experience of halos around lights.

A need exists, therefore, for a material that could mimic the natural lens of the eye and thus eliminate the need for reading glasses after cataract surgery. Such a material must be able to change its shape within the eye and thereby its refractive power. In addition to being used as an IOL in cataract surgery, such a material could also be used to treat other refractive errors including presbyopia (the physiologic loss of accommodation in the eyes due to advancing age).

Injectable, in situ forming gels have several potential uses in medicine, e.g., in intra-ocular lenses, as vitreous substitutes, and as drug delivery devices. In general, in situ forming gels have the advantage of being minimally invasive, easily deliverable, and able to fill native or potential cavities while conforming to different shapes, which may otherwise be difficult to prefabricate. The mechanism of gelation may be physical (changes in temperature, hydrogen bonding, hydrophobic interactions) or chemical (ionic or covalent bond formation). Usually, physical crosslinks are less stable than chemical ones. In situ gelation, resulting in networks covalently crosslinked through free-radical polymerization, may be initiated by heat, chemical initiators, or absorption of photons. Free-radical polymerization, however, is seldom quantitative: the resulting gel usually contains significant amounts of unreacted monomers, initiator, and accelerators—some or all of which may be toxic, and the reaction itself may be very exothermic. For ophthalmic applications in particular the requirements are stringent, and include a narrow range of reaction temperatures very close to ambient, optically clear material, very low chemical and photo-toxicity, and long-term stability in a wet, oxygenated, and photon-rich environment. The aim of the present invention in forming in situ gels is to develop new vitreous substitutes and injectable intraocular lens materials.

Accommodation is a dynamic process by which the refractive power of the optical system, principally the lens, is automatically adjusted to focus light on the retina. This ability is significantly decreased, usually by the fourth decade of life, and lost almost completely by the seventh decade of life through a progressive change in the volume and the elasticity of the lens resulting in an inability to focus on objects closer than arms length, a condition called presbyopia. Evacuating the capsular bag's contents and refilling it with an appropriate volume of a suitable material also offers a potential to restore accommodation to the presbyopic patient. Development of surgical procedures to evacuate the lens capsular bag through a small opening and identification of a suitable material to re-fill the capsular bag has been investigated. Such materials preferably have several advantages, including restoration of accommodation, a smaller corneoscleral incision than now required for semirigid replacement lenses,